GOVERNMENT SUPPORT

This invention was made with government support under Grant Number NIH-2P01-HL41484 awarded by the National Institutes of Health. The government has certain rights in the invention.

In the Claims

Please cancel Claims 1-25.

Please add Claims 26-71 shown below:

26. A molecularly-mediated cardiac pacemaker construct comprising at least one gene that upregulates heart rate or alters cardiac rhythm suitable for localized gene expression in mammalian cardiac atrial tissue.

27. The cardiac pacemaker of Claim 26 wherein gene expression is localized to the sinoatrial node region of the right atria.

28. The cardiac pacemaker of Claim 27 wherein the gene is selected from the group consisting of: a β_2AR gene, β_1AR gene, and $G_{\alpha s}$ gene.

29. The cardiac pacemaker of Claim 28 wherein the construct further comprises expression control elements.

30. The cardiac pacemaker of Claim 29 wherein the expression control element directs transient expression.

31. The cardiac pacemaker of Claim 30 wherein the gene is selected from the group consisting of: a β_2AR gene, β_1AR gene, and $G_{\alpha s}$ gene.

32. The cardiac pacemaker of Claim 31 further wherein the cell is isogenic, allogenic, or xenogenic.

33. A method of regulating cardiac paecmaking activity in a mammal by introducing a biologic pacemaker according to Claim 7 into the sinoatrial node region of a mammalian heart.

34. The method of Claim 33 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

35. A method of improving cardiac function in senescent heart tissue by introducing a biological pacemaker according to Claim 32 into an atrial chamber of a mammalian heart.

36. The method of Claim 35 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

37. The method of Claim 36 wherein the biological pacemaker is a molecular-mediated cardiac pacemaker construct comprising a gene encoding a β2-adrenergic receptor, and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

38. The method of Claim 36 wherein the adrenergic agonist is isoproterenol.

39. The method of Claim 35 wherein the biological pacemaker is a cellular-based cardiac pacemaker construct comprising a transfected or transduced cell expressing a β2-adrenergic receptor and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

40. The method of Claim 39 wherein the adrenergic agonist is isoproterenol.

41. The method of Claim 39 wherein the transfected or transduced cell comprises at least one fetal or embryonic cardiomyocyte transfected with at least one gene that upregulates heart rate or alters cardiac rhythm.

42. A method of improving inotropic responsiveness in a mammal with a cardiac conductive tissue dysfunction by introducing a biologic pacemaker according to Claim 32 into the sinoatrial node region of a mammalian heart.

43. The cardiac pacemaker of Claim 29 wherein the expression control element directs stable expression.

44. A method of improving inotropic responsiveness in a mammal with a cardiac conductive tissue dysfunction by introducing a biologic pacemaker according to Claim 43 into the sinoatrial node region of a mammalian heart.

45. The cardiac pacemaker of Claim 43, wherein the expression control element comprises an inducible promoter.

46. A method of regulating cardiac pacemaking activity in a mammal by introducing a biologic pacemaker according to Claim 20 into the sinoatrial node region of a mammalian heart.

47. The method of Claim 46 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

48. A method of improving cardiac function in senescent heart tissue by introducing a biological pacemaker according to Claim 45 into an atrial chamber of a mammalian heart.

49. The method of Claim 48 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

50. The method of Claim 49 wherein the biological pacemaker is a molecular-mediated cardiac pacemaker construct comprising a gene encoding a β2-adrenergic receptor, and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

51. The method of Claim 49 wherein the adrenergic agonist is isoproterenol.

52. The method of Claim 48 wherein the biological pacemaker is a cellular-based cardiac pacemaker construct comprising a transfected or transduced cell expressing a β2-adrenergic receptor and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

53. The method of Claim 52 wherein the adrenergic agonist is isoproterenol.

54. The method of Claim 52 wherein the transfected or transduced cell comprises at least one fetal or embryonic cardiomyocyte transfected with at least one gene that upregulates heart rate or alters cardiac rhythm.

55. A method of improving inotropic responsiveness in a mammal with a cardiac conductive tissue dysfunction by introducing a biologic pacemaker according to Claim 45 into the sinoatrial node region of a mammalian heart.

56. A cellular-based cardiac pacemaker comprising at least one cell transfected or transduced with at least one gene that upregulates heart rate or alters cardiac rhythm.

57. The cardiac pacemaker of Claim 56 wherein the cell is selected from the group consisting of: a myoblast, a cardiomyocyte, a skeletal muscle myoblast, a fetal or embryonic cardiomyocyte and a cardiac-derived cell line.

58. A method of regulating cardiac pacemaking activity in a mammal by introducing a biologic pacemaker according to Claim 31 into the sinoatrial node region of a mammalian heart.

59. The method of Claim 58 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

60. A method of improving cardiac function in senescent heart tissue by introducing a biological pacemaker according to Claim 56 into an atrial chamber of a mammalian heart.

61. The method of Claim 60 wherein the biological pacemaker is introduced by direct myocardial injection or endocardiac transfection or transduction.

62. The method of Claim 61 wherein the biological pacemaker is a molecular-mediated cardiac pacemaker construct comprising a gene encoding a β2-adrenergic receptor, and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

63. The method of Claim 61 wherein the adrenergic agonist is isoproterenol.

64. The method of Claim 60 wherein the biological pacemaker is a cellular-based cardiac pacemaker construct comprising a transfected or transduced cell expressing a β2-adrenergic receptor and further wherein the method comprises *in vivo* administration of an adrenergic agonist.

65. The method of Claim 64 wherein the adrenergic agonist is isoproterenol.

66. The method of Claim 64 wherein the transfected or transduced cell comprises at least one fetal or embryonic cardiomyocyte transfected with at least one gene that upregulates heart rate or alters cardiac rhythm.

67. A method of improving inotropic responsiveness in a mammal with a cardiac conductive tissue dysfunction by introducing a biologic pacemaker according to Claim 56 into the sinoatrial node region of a mammalian heart.

68. A method of treating a mammal suffering from a heart attack or transient depression of heart rate by delivering to the mammal a transient molecularly-mediated cardiac pacemaker.

69. A method of permanently regulating cardiac pacemaking activity in a mammal by introducing a cellular-based cardiac pacemaker comprising at least one fetal or embryonic cardiomyocyte transfected or transduced with at least one gene that upregulates heart rate or alters cardiac rhythm.

70. A method of permanently regulating cardiac pacemaking activity in a mammal by introducing a molecularly-mediated cardiac pacemaker construct comprising at least one gene that upregulates heart rate or alters cardiac rhythm suitable for localized stable gene expression in mammalian cardiac atrial tissue.

71. The method of Claim 70 wherein the molecularly-mediated cardiac pacemaker construct comprises an inducible promoter.